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P1 1019776

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

June 06, 2003

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE.

APPLICATION NUMBER: *60/376,498*
FILING DATE: *April 30, 2002*
RELATED PCT APPLICATION NUMBER: *PCT/US03/13560*

By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS

T. Wallace
T. WALLACE
Certifying Officer

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Express Mail Label No.: EV 092 [redacted] 030 US

PATENT

Attorney Docket No.: AVOIR-07217

PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 C.F.R. 1.53(b)(2).

Docket Number	AVIOR-07217	Type a plus sign (+) inside this box →	+

INVENTOR(s) / APPLICANT(s)

Last Name	First Name	Middle Initial	Residence (City and Either State or Foreign Country)
Lieber	Andre		Seattle, WA

TITLE OF THE INVENTION (280 Characters Max.)

Kits, Systems, Compositions, and Methods for Dendritic Cell Transduction, Maturation, and Stimulation of Antigen Specific Immune Responses.

CORRESPONDENCE ADDRESS

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
United States of America

ENCLOSED APPLICATION PARTS *(Check All That Apply)*

X	Specification	Number of Pages	1	___	Small Entity Statement
X	Drawing(s)	*Number of Sheets*	0	___	Other (Specify): Power of Attorney
				___	Other (Specify): Assignment

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

___	Charge Account No. **08-1290** in the amount of **$80.00. An originally executed duplicate of this transmittal is enclosed for this purpose.**	FILING FEE AMOUNT ($)	**$80.00**
X	The Commissioner is hereby authorized to charge any deficiency in the payment of the required fee(s) and/or credit any overpayment to Deposit Account No.: **08-1290. An originally executed duplicate of this transmittal is enclosed for this purpose.**		

This invention was made by an agency of the United States Government under a contract with an agency of the United States Government.

X No.
___ Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

Date: April 30, 2002

Jason R. Bond
Reg. No.: 45,439
MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
(608) 218-6900

___ Additional inventors are being named on separately numbered sheets attached hereto.

Express Mail Label No.: [redacted]092 300 030 US

[redacted]

PATENT
Attorney Docket No.: **AVIOR-07217**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Andre Lieber

For: **Kits, Systems, Compositions, and Methods for Dendritic Cell Transduction, Maturation, and Stimulation of Antigen Specific Immune Responses.**

Box Provisional Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATION UNDER 37 C.F.R. § 1.10

I hereby certify that this correspondence and the documents referred to as attached therein are being deposited with the United States Postal Service on **April 30, 2002**, in an envelope as "EXPRESS MAIL POST OFFICE TO ADDRESSEE" service under 37 C.F.R. § 1.10, Mailing Label Number **EV 092 300 030 US** addressed to: **Box Provisional Patent Application**, Assistant Commissioner for Patents, Washington, D.C. 20231.

Susan M. McClintock
Susan M. McClintock

TRANSMITTAL COVER SHEET FOR FILING PROVISIONAL APPLICATION (37 C.F.R. § 1.51(2)(i))

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 C.F.R. 1.53(b)(2).

1. The following comprises the information required by 37 C.F.R. § 1.51(a)(2)(i)(A):

2. The name(s) of the inventor(s) is/are (37 C.F.R. § 1.51(a)(2)(i)(B)):

   Andre Lieber

3. Address(es) of the inventor(s), as numbered above (37 C.F.R. § 1.51(a)(2)(i)(C)):

   Seattle, WA

4. The title of the invention is (37 C.F.R. § 1.51(a)(2)(i)(D)):

   Kits, Systems, Compositions, and Methods for Dendritic Cell Transduction, Maturation, and Stimulation of Antigen Specific Immune Responses.

5. The name, registration, and telephone number of the attorney (*if applicable*) is (37 C.F.R. § 1.51(a)(2)(i)(E)):

   Jason R. Bond
   Reg. No.: 45,439
   Tel.: (608) 218-6900

(complete the following, if applicable)

___ A Power of Attorney accompanies this cover sheet.

6. The docket number used to identify this application is (37 C.F.R. § 1.51(a)(2)(i)(F)):

Docket No.: **AVIOR-07217**

7. The correspondence address for this application is (37 C.F.R. § 1.51(a)(2)(i)(G)):

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105

8. Statement as to whether invention was made by an agency of the U.S. Government or under contract with an agency of the U.S. Government. (37 C.F.R. § 1.51(a)(2)(i)(H)):

This invention was made by an agency of the United States Government, or under contract with an agency of the United States Government.

X No.

___ Yes.

The name of the U.S. Government agency and the Government contract number are:

9. Identification of documents accompanying this cover sheet:

A. Documents required by 37 C.F.R. § 1.51(a)(2)(ii)-(iii):

Specification: No. of pages **1**

Drawings: No. of sheets **0**

B. Additional documents:

___ Claims: No. of claims

___ Power of Attorney

___ Small Entity Statement

___ Assignment

___ Other

10. Fee

The filing fee for this provisional application, as set in 37 C.F.R. § 1.16(k), is $160.00, for other than a small entity, and $80.00, for a small entity.

X Applicant is a small entity.

11. Small Entity Statement

___ The verified statement(s) that this is a filing by a small entity under 37 C.F.R. §§ 1.9 and 1.27 is(are) attached.

12. Fee payment being made at this time

__ Charge Account No. **08-1290** in the amount of **$80.00. An originally executed duplicate of this transmittal is enclosed for this purpose.**

13. Method of Fee Payment:

_X_ Check in the amount of **$80.00**

____ Charge Account No. **08-1290,** in the amount of **$80.00. A duplicate of this Cover Sheet is attached.**

_X_ Please charge Account No. **08-1290** for any fee deficiency. **A duplicate of this Cover Sheet is attached.**

Date: April 30, 2002

Jason R. Bond
Reg. No.: 45,439

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
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(415) 904-6500

Kits, Systems, Compositions, and Methods for Dendritic Cell Transduction, Maturation, and Stimulation of Antigen Specific Immune Responses.

Transduction of Human CD34+ Peripheral Blood Derived Dendritic Cells with a Model Tumour Antigen is More Efficient with Chimeric Ad5/11 and Ad5/35 Adenoviruses than Ad5

In order to use dendritic cells as immunotherapy vectors, an efficient method of antigen delivery is essential. Subgroup C (serotype 5) based adenovirus vectors have successfully been used to transduce human dendritic cells (DC) in culture, however the need for high MOI's and the resulting toxicity has hindered their use. Following our previous observation that Ad 5 based vectors possessing group B fibers (Ad11 and Ad35) give increased transduction over Ad5 vectors in human hematopoetic cells without abhorrent toxicity, we investigated the transduction efficiencies of these vectors in human hematopoetic derived DCs. Infection of immature CD11c positive DCs derived from peripheral CD34+ cells, with Ad5, Ad5/11 and Ad5/35 vectors expressing GFP resulted in <1%, 59% and 37% transduction at an MOI of 5. Maximal transduction efficiency with Ad5/11 and Ad5/35 vectors (85-95%) was achieved at a MOI 100 whilst only 58% transduction was achieved with the highest Ad5 dose tested (MOI 1000). Expression of the DC maturation markers CD86, CD83 and HLA-DR was seen to increase upon Ad5/11 and Ad5/35, but not Ad5 infection, 24 hours after infection. Furthermore introduction of the maturation factor (LPS) to infected DCs resulted in an increased percentage of cells expressing GFP following Ad5/11 and Ad5/35, but not Ad5, infection. Ad5 and Ad5/35 vectors were then generated expressing a model tumour antigen (Hepatitis B nucleocapsid, HBeAg) from a *RETROGEN* cassette that contains an N-terminal leader sequence and a C-terminal human Fc binding domain. Ad5/35 infected CD11c positive DCs showed enhanced expression of HBeAgFC compared to the Ad5 infected cells. Ad5 and Ad5/35 HBeAgFc infected DCs were then incubated with antigen loaded autologous peripheral T cells. Enhanced T cell proliferation and secretion of the Th1 cytokine IFN-γ was seen in T cells incubated with Ad5/35HBeAgFc infected DCs compared to Ad5HBeAgFc infected cells. Taken together these results indicate that group B pseudotyped adenoviruses enable more efficient DC transduction, maturation and stimulation of antigen specific immune responses at lower, not toxic MOIs.